EXAMPLE 19

Preparation of 5'-*O*-DMT-3'-O-[hexyl-(6-phthalimido)]-uridine-2'-O-succinoyl-aminopropyl CPG

[0154] Succinylated and capped aminopropyl controlled pore glass (CPG; 500Å pore diameter, aminopropyl CPG, 1.0 grams prepared according to Damha *et. al., Nucl. Acids Res.* **1990**, *18*, 3813.) was added to 12 mL anhydrous pyridine in a 100 mL round-bottom flask. 1-(3-Dimethylaminopropyl)-3-ethyl-carbodiimide (DEC; 0.38 grams, 2.0 mmol)], triethylamine (TEA; 100 µl, distilled over CaH_2), dimethylaminopyridine (DMAP; 0.012 grams, 0.1 mmol) and nucleoside 5'-O-DMT-3'-O-[hexyl-(6-phthalimido)]uridine (0.6 grams, 0.77 mmol) were added under argon and the mixture shaken mechanically for 2 hours. Additional nucleoside (0.20 grams) was added and the mixture shaken for 24 hours. The CPG was filtered off and washed successively with dichloromethane, triethylamine, and dichloromethane. The CPG was then dried under vacuum, suspended in 10 mL piperidine and shaken 15 minutes. The CPG was filtered off, washed thoroughly with dichloromethane and again dried under vacuum. The extent of loading (determined by spectrophotometric assay of DMT cation in 0.3 M p-toluenesulfonic acid at 498 nm) was approximately 28 µmol/g. The 5'-O-(DMT)-3'-O-[hexyl-(6-phthalimido] uridine-2'-O-succinyl-aminopropyl controlled pore glass was used to synthesize the oligomers in an ABI 380B DNA synthesizer using phosphoramidite chemistry standard conditions. A four base oligomer 5'-GACU*-3' was used to confirm the structure of 3'-O-hexylamine tether introduced into the oligonucleotide by NMR. As expected a multiplet signal was observed between 1.0-1.8 ppm in ^1H NMR.

EXAMPLE 20

5'-*O*-DMT-3'-O-[hexylamino]-uridine

[0155] 5'-O-(DMT)-3'-O-[hexyl-(6-phthalimido)] uridine (4.5 grams, 5.8 mmol) is dissolved in 200 mL methanol in a 500 mL flask. Hydrazine (1 ml, 31 mmol) is added to the stirring reaction mixture. The mixture is heated to 60-65 °C in an oil bath and refluxed 14 hours. The solvent is evaporated *in vacuo* and the residue is dissolved in dichloromethane (250 mL) and extracted twice with an equal volume NH_4OH. The organic layer is evaporated to yield the crude product which NMR indicates is not completely pure. R_f=0 in 100% ethyl acetate. The product is used in subsequent reactions without further purification.

EXAMPLE 21

3'-O-[Propyl-(3-phthalimido)]-adenosine

[0156] To a solution of adenosine (20.0 g, 75 mmol) in dry dimethylformamide (550 ml) at 5 °C was added sodium hydride (60% oil, 4.5 g, 112 mmol). After one hour, N-(3-bromopropyl)-phthalimide (23.6 g, 86 mmol) was added and the temperature was raised to 30 °C and held for 16 hours. Ice is added and the solution evaporated *in vacuo* to a gum. The gum was partitioned between water and ethyl acetate (4 x 300 mL). The organic phase was separated, dried, and evaporated *in vacuo* and the resultant gum chromatographed on silica gel (95/5 CH_2Cl_2/MeOH) to give a white solid (5.7 g) of the 2'-*O*-(propylphthalimide)adenosine. Thee fractions containing the

3'-*O*-(propylphthalimide)adenosine were chromatographed a second time on silica gel using the same solvent system.

[0157] Crystallization of the 2'-*O*-(propylphthalimide)adenosine fractions from methanol gave a crystalline solid, m.p. 123-124C. ^{1}H NMR (400 MHZ: DMSO-d_6) δ 1.70(m, 2H, CH_2), 3.4-3.7 (m, 6H, C_5, CH_2, OCH_2, Phth CH_2), 3.95 (q, 1H, C_4H), 4.30 (q, 1H, C_5H), 4.46 (t, 1H, C_5H), 5.15 (d, 1H, C_3OH), 5.41 (t, 1H, C_5OH), 5.95 (d, 1H, C_1H) 7.35 (s, 2H, NH_2), 7.8 (brs, 4H, Ar), 8.08 (s, 1H, C_2H) and 8.37 (s, 1H, C_8H). Anal. Calcd. $C_{21}H_{22}N_6O_6$: C, 55.03; H, 4.88; N, 18.49. Found: C, 55.38; H, 4.85; N, 18.46.

[0158] Crystallization of the 3'-*O*-(propylphthalimide)adenosine fractions from H_2O afforded an analytical sample, m.p. 178-179C. ^{1}H NMR (400 MHZ: DMSO-d_6) δ 5.86 (d, 1H, H-1').

EXAMPLE 22

3'-O-[Propyl-(3-phthalimido)]-N6-benzoyl-adenosine

[0159] 3'-*O*-(3-propylphthalimide)adenosine is treated with benzoyl chloride in a manner similar to the procedure of Gaffney, *et al.*, *Tetrahedron Lett.* **1982**, *23*, 2257. Purification of crude material by chromatography on silica gel (ethyl acetate-methanol) gives the title compound.

EXAMPLE 23

3'-O-[Propyl-(3-phthalimido)]-5'-O-DMT-N6-benzoyl-adenosine

[0160] To a solution of 3'-O-(propyl-3-phthalimide)-N^6-benzoyladenosine (4.0 g) in pyridine